

identified herein as tick-derived protease inhibitor protein (TdPI), an active fragment thereof or a functional equivalent thereof. This sequence is given in accompanying Figure 1 (SEQ.ID.NO:2). This protein was identified as being encoded by a cDNA from a tick salivary gland library. The protein has a molecular weight of approximately 13.5 kDa and appears to belong to the family of Kunitz-type protease inhibitors. The sequence similarity with other members of this family such as aprotinin and inter-alpha-trypsin inhibitor is low, but the putative reactive centre and the position of the cysteines is to some extent conserved.--

Please replace the paragraphs at Page 8, Lines 20-22 and 23-29, respectively, with the following

--A cDNA encoding TdPI is disclosed herein by way of example and its sequence and the amino acid sequence it encodes are shown in Figure 1 (nucleotides (SEQ ID NO:1) and amino acids (SEQ ID NO:2) are given in their standard one letter abbreviations).

A preferred nucleic acid molecule according to the invention comprises a nucleotide sequence identical to or complementary to the sequence shown in Figure 1 (SEQ ID NO:1), or a sequence that is degenerate or substantially homologous therewith, or which hybridises with this sequence under non-stringent conditions, for instance 6 x SSC/50% formamide at room temperature, and washed under conditions of low stringency, for instance (2 x SSC room temperature or 2 x SSC, 42°C or, more preferably, binding under conditions of higher stringency, e.g. 2 x SSC, 65°C. (SSC = 0.15M NaCl, 0.015M sodium citrate, pH 7.2).--

Please replace the paragraphs at Page 10, lines 19-20 and 23-26, respectively, with the following:

--Figure 1 shows the cDNA sequence (SEQ ID NO:1) and inferred amino-acid sequence (SEQ ID NO:2) of TdPI-encoding clone 76-3.

Figure 3 shows an alignment of TdPI (SEQ ID NO:2) with Kunitz domains of the bovine

colostrum trypsin inhibitor (SEQ ID NO:3) (BovCol; Cechova, 1976), (bovine) aprotinin (SEQ ID NO:5) (Creighton & Charles, 1987), and the rat tissue factor pathway inhibitor (TFPI-2 (SEQ ID NO:4); only the second, factor Xa-inhibiting domain is shown; Enjyoji *et al.*, 1992).--

Please replace the paragraph from Page 12, Line 16 to Page 13, line2, with the following:

--Recombinant TdPI (rTdPI) was expressed as a histidine-tagged protein in *Spodoptera frugiperda* ovarian cells (SJ21; Invitrogen). The coding region of the TdPI cDNA was amplified by the polymerase chain reaction (PCR), using the forward primer

5'-GCAGGAGCTCGGCACGAG (SEQ ID NO:9)

and the reverse primer

5'-TATGGATCCCAGGTCCAGGCTCTGTTCCG (SEQ ID NO:10),

thereby adding a *Sac* I site upstream of the start codon, and replacing the stop codon with a *Bam* HI site. The PCR consisted of 20 cycles with a 30-second melting step (95°C) a 30-second primer-annealing step (50°C) and a 30-second extension step (72°C). The PCR product was ligated between the *Sac* I and *Bam* HI sites of the pAC129.1 transfer vector (Livingstone & Jones, 1989), which was modified so that a carboxyterminal Gly-Ile-(His)₆ tag was added to the expressed protein. Co-transfection of SJ21 cells with the transfer vector and baculovirus (BacPak6) and amplification of recombinant virus was as described by Kitts & Possee, 1993. rTdPI was expressed in TC100 medium (Gibco BRL) containing 10% foetal bovine serum (Sigma).--

Please replace the paragraph from Page 14, Lines 4-16 with the following: